Evaluation of a Visualization-based Approach to Functional Brain Mapping

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We describe a method for mapping stimulation data, obtained at the time of neurosurgery for intractable epilepsy, onto a 3D MRI-based neuroanatomic model of the individual patient. The mapping is done by comparing an intraoperative photograph of the exposed cortical surface with a computer-based MR visualization of the surface, interactively indicating corresponding stimulation sites, and recording 3-D MR machine coordinates of the indicated sites. Repeatability studies were performed to validate the accuracy of the mapping technique. Six observers - a neurosurgeon, a radiologist, and four computer scientists, independently mapped 218 stimulation sites from 12 patients. The mean distance of the six locations from the mean location of each site was 2.07 *mm, with a standard deviation of* 1.5 *mm, or within* 5.07 *mm with* 95% *confidence. Since the surgical sites are accurate within approximately 1 cm, these results show that the visualization-based approach is accurate within the limits of the stimulation maps. When incorporated within the kind of information system envisioned by the Human Brain Project, this anatomically-based method will not only provide a key link between non-invasive and invasive approaches to understanding language organization, but will also provide the basis for studying the relationship between language function and anatomical variability.*

INTRODUCTION

Cortical language maps obtained through intraoperative electrical stimulation studies provide a rich source of information for research on language organization. Through stimulation studies, cortical sites essential for language function can be identified and thereby avoided during surgery. Non-computer-based studies have shown interesting correlations between the distribution of these essential language sites and such behavioral indicators as verbal IQ.[7] These empirical observations lead to interesting speculations about whether distribution of language, or any other function, can be related to variations in cortical anatomy and whether function can be predicted from anatomy alone. Further validation of this apparent relationship between function and anatomy could be made possible by the integration of stimulation data with data from other modalities such as fMRI, PET, SPECT, and ECoG.

To date, there has been no study on techniques that would enable the integration of electrical stimulation data obtained invasively with functional data obtained from non-invasive sources such as fMRI and PET. If surgical data can be integrated with non-invasive functional methods, and if the language areas as revealed by the two methods are found to be highly correlated, it may be possible to altogether supplant intraoperative studies with the more convenient non-invasive methods.

In a previous article,[5] we introduced our volume-based visualization approach to integrating these two sources of data: an MR-based volume rendering of the patient's left temporal cortex is created by combining three separate MR-volume datasets, optimized respectively for cortical anatomy, veins, and arteries. The combined rendering is compared with an intraoperative photograph of the exposed cortical surface showing the location of sites tested for language. An interactive tool is used to drag numbered icons and place them at locations on the rendering that correspond to the sites on the photograph. The 3D MR-machine coordinates of the mapped sites are then stored in a database, thereby allowing them to be related to other MR-based sources of language data.

In the current article we describe an improved surface-based visualization scheme that has (a) produced more detailed reconstructions of the brain and blood vessels than the previous volume-based approach, and (b) enabled the unambiguous mapping of all the 218 stimulation sites in our 12-patient data set. We also describe mapping repeatability experiments that demonstrate that our technique is now accurate enough to be used in integrating multiple sources of data about language organization.

VISUALIZATION-BASED FUNCTIONAL MAPPING

Identification of cortical sites essential for language function is necessary in order to plan resection for the treatment of left temporal tumor or intractable epilepsy. In the work of Ojemann et al.,[7] language data are obtained at the time of neurosurgery via electrical stimulation mapping. The stimulation studies are done for an object naming task, although other tasks are used on a subset of patients. After the initial craniotomy has been performed, an initial set of sites chosen for stimulation study is marked with numbered tags placed on the exposed cortical surface. The awake patient is now shown slides of familiar objects, such as planes, boats, and trees, and is required to perform object naming. For every other slide, the neurosurgeon applies a small electric current (1.5 to 10 mA) to the selected numbered sites, for a total of approximately 3 stimulations per site. If the stimulation of a site leads to object naming errors at least two times out of three, even though the patient can name the object correctly in the absence of any stimulation, the site is determined to be essential for language function and is thereby avoided during surgery.

Given a photograph showing the location of these stimulation sites (Figure 3), and the record of which sites are essential for language, the task now becomes one of relating these sites to the MR machine coordinate system. The visual comparison approach we are developing requires that a detailed rendering of the cortical surface and superficial blood vessels be obtained so that features on the photograph can be matched, by the human expert, with those on the rendering. Once the features have been matched, the mapping process involves dragging numbered icons indicating site numbers using the computer mouse, and placing them at the appropriate location on the 3D reconstruction of the cortex. The 3D machine coordinates of the mapped sites, and other associated information, are then stored in a web-based repository,[4] which is a form of multimedia database system.

In our earlier work,[5] we described a volume-based approach to visualization. Further experience showed that the cortical anatomy and vessels were often not distinct enough to be useful for unambiguous identification of site locations. The surface-based scheme we describe in this article provides much more detailed reconstructions that lead to unambiguous mappings. As in the previous work, our heterogenous software environment consists of Advanced Visual Systems' AVS, a commercial data visualization package, and Skandha4, an in-house graphics program.

Surface Visualization

The approach we take to extracting surfaces from volume data is to use *region grow*, a region growing algorithm,[6] to derive a region-of-interest (ROI) mask for cortical data. The mask is used to exclude non-cortical tissue from the volume data before running a generic isosurface algorithm provided by AVS, called *isosurface*, to produce the cortical surface. The surface renderer used is part of the AVS module *geometry viewer*. The AVS network that is used to extract the cortical, venous, and arterial isosurfaces is shown in Figure 1. The two AVS volumes read in to the network are the tissue (cortex, vein, or artery) volume, and the ROI mask produced by *region grow*. The ROI mask, which appears on the left in the AVS network, is processed first by a morphological opening operation. Implemented as an erosion followed by a dilation, the opening of the ROI mask with a 20-pixel-wide disk structuring element, supplied by the *ip read sel* module, smooths the mask and gets rid of narrow leakages. The opening operation is followed by an additional dilation by a cross structuring element, whose size and the number of dilation iterations are controlled interactively to produce a mask that just encloses the cortical data and excludes the scalp and other structures. The masked volume data is produced by multiplying the volume data with the ROI mask data. The *isosurface* module is used to extract the cortical, venous, and arterial surface, which is then displayed using the *geometry viewer* renderer.

Intensity Inhomogeneity Correction

Some of our earlier MR image series (9415, 9411, 9451, and 9410) were obtained using a temporal phased-array coil centered over the sylvian fissure of the patient, bilaterally. The increased signal-to-noise ratio was obtained at the cost of an inhomogeneity artifact. This artifact manifests itself as an intensity fall off across the volume data. The surface rendering process requires that voxels belonging to the tissue of interest have roughly the same intensity value. The isosurface rendering of patient 9415, with an isosurface threshold value optimized for the left temporal cortical surface, is shown in Figure 2(a).

The RF inhomogeneity present in the earlier datasets can be modeled as a low frequency signal in contrast to the high frequency information present in the underlying anatomy. We found that a simple homomorphic filtering was sufficient to remove the gradient artifact. The intensity gradient is modeled as a multiplicative, low-frequency noise factor. Thus, the observed signal is considered a product of the original signal with the noise factor. A 19-pixel-wide square kernel is used to convolve the original image slices and produce a low frequency image. By taking the logarithm of the observed image and subtracting the low-pass filtered signal from the log image, the multiplicative noise factor can be separated out. The log image is then exponentiated to get the final output image which has been rid of the intensity fall off artifact. Figure 2(b) shows the isosurface extracted from the gradient-corrected dataset.

Language Mapping

Language site mapping is done using the Skandha4 package. The three surface models produced by AVS (one each for cortex, veins, and arteries), the corresponding intraoperative photograph, and the original MR volume data, are loaded into the language mapping module. Skandha4 controls, similar to those in the AVS *Geometry Viewer* module, are used to manipulate color, lighting, surface properties, and viewpoint of the rendered models. The language site mapping is done interactively, with the vasculature and the cortical surface features guiding the user in the accurate localization of the language sites. After the mapping is complete, the stimulation sites and their corresponding 3D coordinates in machine space are stored for that particular patient.

The mapping data are stored in the multimedia database system described elsewhere.[4] Using Perl scripts that incorporate SQL queries, the mapping data corresponding to maps produced by the different mappers are extracted from the repository, and repeatability statisitics are computed.

REPEATABILITY RESULTS

The visual comparison approach was utilized to map stimulation sites of our first set of 12 patients. Repeatability experiments were performed using two groups of mappers - an expert group consisting of a neurosurgeon (GO) and a neuro radiologist (KM), and a non-expert group consisting of four computer scientists involved in various stages of this project. The mappings were all done independently in a couple of sittings within a week. The time required to map a particular patient depended on the number of stimulation sites and usually varied from 15 to 30 minutes. Since the intraoperative photo and the rendering did not always have identical aspect and scale, locating landmarks - the initial step employed by all mappers - was time consuming in some cases (e.g: 9602, 9612). Critical cortical landmarks were sometimes not clearly visible because of the poor quality of intraoperative photographs. In many of the patients, not all the stimulation sites were mapped by all the mappers because the numbered stickers on the sites were not clearly visible (9410).

For each stimulation site, the mean of the two expert mappings was considered to be the gold standard or the "true" site location. The distances, in three dimensions, of non-expert mappings from this gold standard were determined. The mean distance of non-expert mappings from the true stimulation site locations was evaluated for each patient. As mentioned before, not every site was mapped by all the mappers. But, for a site to be included in the statistical evaluation, both experts and at least one of the four non-expert mappers should have mapped it. Figure 4 summarizes the results for each patient dataset and the overall mean and standard deviation of the distance of non-expert mappings from true stimulation site locations. Figure 4 also summarizes the variability within the expert group.

A two-mean t test, at 0.05 significance, reveals that the mean distance of non-expert mappings from the gold standard exceeds the mean distance within the expert group. This suggests a difference between the quality of mappings obtainable by experts and non-experts, with experts faring slightly better than the non-experts. However, more experts are needed to verify this conclusion. With a probability of 0.95, the non-expert mappings fall within a distance of 6.781 mm $(2.87 + 2 \times 1.95)$ from the true stimulation site location (4.227 mm for the expert group). Since the language areas and distances between sites are accurate to one cm, the accuracies achievable by our method are satisfactory.

We also evaluated the statistics for the various mappings when the experts and non-experts are not differentiated. The true site locations, instead of being the mean of expert mappings, now becomes the mean of all the mappings. The mean distance of a mapping from the corresponding "true" site location is 2.07 *mm*, with a standard deviation of 1.49 *mm*, or within 5.07 *mm* (2.07+2x1.49) at 0.95 confidence.

DISCUSSION AND CONCLUSIONS

This paper has described a surface-based visualization approach to mapping intraoperative stimulation data onto a 3D MRI-based neuroanatomic model of the individual patient. The mapping is done by comparing an intraoperative photograph of the exposed cortical surface to a computer-generated visualization of the 3-D model, then interactively indicating the location on the model of stimulation sites visible on the photograph. Repeatability studies by 6 observers on 12 patients containing 218 sites show that the sites are accurate within 5.07 mm, with no major differences between experts and non-experts, although more experts are needed to verify this. Since the stimulation sites are only accurate within 1 *cm*,[7] the visualization-based approach is adequate within the limits of the surgical technique. Further developments in segmentation and visualization will only improve this accuracy.

The 3-D MR machine coordinates provided by the visualization-based mapping technique are the key link between invasive stimulation data and non-invasive methods such as fMRI, PET and ECoG, since methods have been developed to register these functional images with MR-based volume datasets. Once these two kinds of data have been related it will be possible to determine whether they are correlated. If they are highly correlated it may be possible to altogether supplant intraoperative studies with the more convenient non-invasive methods. The 3-D coordinates also allow us to combine data from multiple patients using methods such as Tailarach coordinates,[9] surface-based coordinates based on major sulcal landmarks,[7] cortical unfolding,[8,2] and atlas deformation.[3,10] These approaches will allow us to further confirm the hypothesis that some but not all of the observed variability in surgical language site distribution can be correlated with anatomic variability.

Although such a demonstration will require many more patients, the method described in this paper provides the key to testing these kinds of hypotheses. Since many patient datasets will be needed an additional requirement is an information management system, which we are currently developing,[4] that can keep track of the large amount of raw and derived image data, as well as stimulation mapping and other clinical data. The system should also allow these data to be related to other language-related information available on the Internet, and should provide methods for visualizing the integrated results. We are currently developing such a system as part of the national Human Brain Project.[1]

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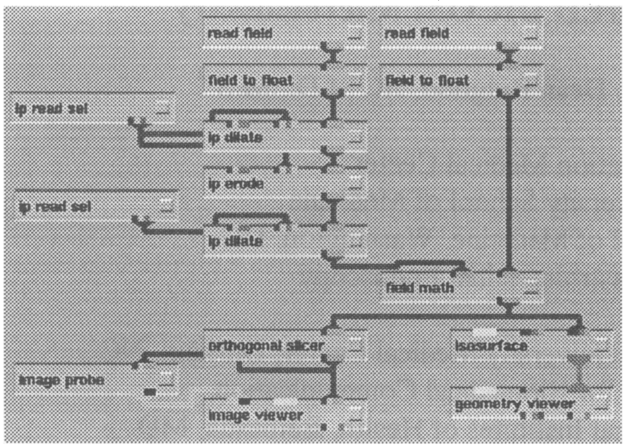

Figure 1: AVS network for isosurface extraction. The volume dataset (cortical, venous, or arterial) is loaded on the right and the ROI mask from region grower on the left. The surface model created by this network is visualized here using the *Geometry Viewer* module.

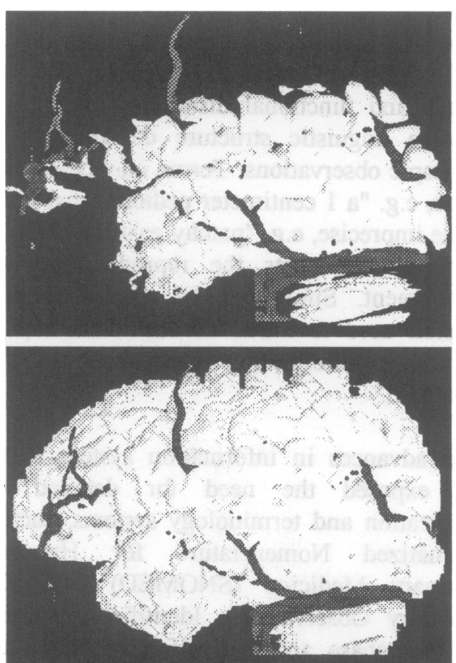

Figure 2: Top: Isosurface rendering of patient 9415 without the gradient correction. Bottom: Isosurface rendering obtained after correction.

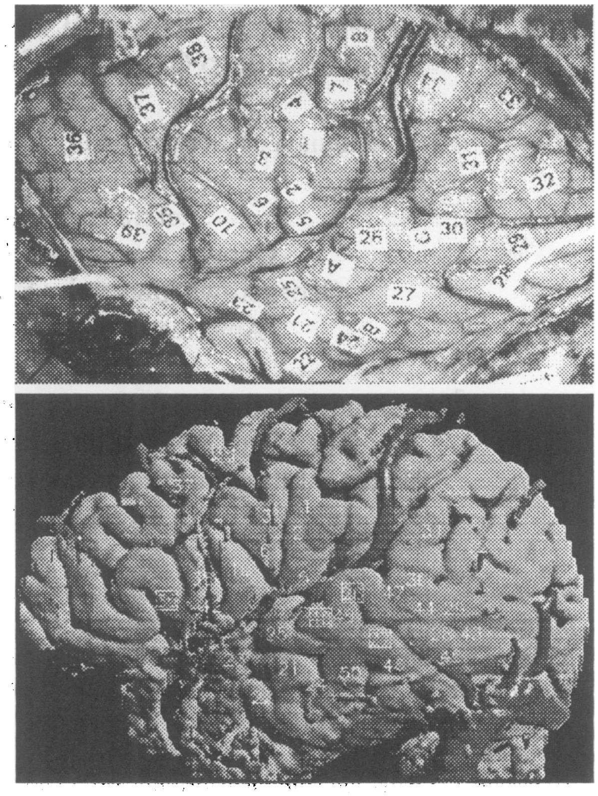

Figure 3: Intraoperative photo and corresponding mapping for patient 9411. Sites shown enclosed in rectangles are essential for language function.

Patient	$\bar{d}_y/\sigma_{d_y}$	n_y	$\bar{d}_z/\sigma_{d_z}$	n_z
9411	2.20/1.36	108	1.48/1.23	54
9415	3.04/2.40	124	1.78/1.43	64
9410	2.71/1.74	71	1.61/1.00	36
9535	2.58/1.43	96	1.42/1.10	48
5988	3.07/1.92	80	2.33/1.71	40
5919	2.82/1.98	84	1.64/1.16	42
9538	2.72/2.14	67	1.27/1.34	34
9602	2.70/1.79	72	1.53/0.67	36
9612	3.18/2.65	75	1.62/1.11	38
9617	3.80/2.27	48	2.50/2.04	26
9618	3.54/2.06	43	1.74/1.13	22
All Patients	2.87/1.95	868	1.69/1.26	440

Figure 4: Repeatability results. $\bar{d}_y$ and σ_y are the mean distance and standard deviation , respectively, of a non-expert mapping from the "true" site location. $\bar{d}_z$ and σ_z are the corresponding quantities for expert mappings. n is the number of mappings. In the absence of a gold standard, the "true" site location is defined as the mean of the expert mappings. All distances are in *mm*.